In situ skeletonized bilateral thoracic artery for left coronary circulation

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Original Article

In-Situ Skeletonized Bilateral Thoracic Artery for Left Coronary Circulation: a 20-Year Experience

Short Title: TAMR

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VISUAL ABSTRACT

Key question: What are the immediate and long-term outcomes when using in-situ skeletonized BITAs for left coronary circulation (LCC)?

Key findings: In-situ skeletonized BITAs to LCC is associated with good long-term outcomes and graft patency

Take-home message: The reported surgical strategy optimizes immediate and long-term results and should be applied extensively in CABG patients.

Abstract

Background. We aimed to analyze the outcomes in a patient population using a standardized technique for coronary artery bypass consisting of total arterial myocardial revascularization with in-situ skeletonized bilateral thoracic artery for left coronary circulation (ISS-LITA-LCC-TAMR). We also explored potential predictors of long-time unfavorable outcomes.

Methods. Patients undergoing ISS-LITA-LCC-TAMR between January 1997 and May 2017, were included prospectively in this study. Median follow-up (100% complete) was 103 months (IQR 61 to 189 months) and ranged from 1 to 245 months.

Results One-thousand-three-hundred-twenty-five consecutive patients were recruited. During follow up there were 131 deaths (9.8%), 146 repeat revascularizations (11.0%) and 229 major adverse cardiac events (MACE, 17.2%). Eighteen-year freedom from these events were 62.6±9.3%,62.5±6.3% and 53.9±11.0 %, respectively. Multivariable models showed that left ventricular ejection fraction ≤ 35%, chronic obstructive pulmonary disease, peripheral vascular disease ($p<0.001$), chronic kidney disease and age ≥80 years ($p=0.002$) were independent predictors of diminished long-term survival. Moreover, peripheral vascular disease and off-pump coronary artery bypass (both, $p<0.001$) predicted repeat revascularization. Finally, age ≥ 80 years, peripheral vascular disease, left ventricular ejection fraction ≤ 35%, off-pump coronary artery bypass and chronic pulmonary obstructive disease were independent predictors of MACE during long-term follow-up (all, $p<0.001$).

Conclusions. Coronary artery bypass using the ISS-LITA-LCC-TAMR configuration resulted in satisfactory long-term results with low incidence of death and late events and may represent a technique of choice in selected CABG patients. Larger and long-term prospective studies are, however, warranted.

Keywords. Internal Thoracic Artery; Arterial Myocardial Revascularization, Coronary artery bypass

Introduction

The use of the left internal thoracic artery (LITA) to revascularize the left anterior descending artery (LAD) has been acknowledged as the gold-standard for coronary artery bypass grafting (CABG) [1]. Moreover, the additional benefits of the use of the right internal thoracic artery (RITA) in a bilateral configuration (BITA) has previously been reported [2–5]. A major issue with BITA use, however, is the risk of sternal complications [6]. Furthermore, many surgeons claim there is not enough evidence to support the use of BITA, mainly due to the conflicting results reported from heterogeneous studies [6–8].

The most recent surgical revascularization guidelines (2018 ESC/EACTS), for example, recommends the use of BITA on the LV coronary circulation as an optimal surgical option and should be considered (class IIa) for appropriate patients. Furthermore employment of the RA as an alternative conduit to the RITA (class IIa), with the skeletonized BITA may also be considered (class IIb) offering improved outcomes in patients with higher risk of infections [9]'

Since 1997 we have utilized a standardized CABG graft configuration for total arterial revascularization. This consists of the in-situ skeletonized BITA for left coronary circulation grafting (ISS-BITA-LCC) with, if necessary, a radial artery (RA) on the right coronary circulation in a total arterial myocardial revascularization (TAMR) configuration (ISS-BITA-LLC-TAMR).

We report our experience over 20 years with this approach and hypothesize that the use of ISS-BITA-LLC-TAMR configuration leads to positive long-term (>20 years) outcomes in terms of survival, repeat revascularization and major adverse cardiac events. We also explored potential predictors of these events.

Methods

Approval was received by the Institutional Ethical Committee due to the prospective analysis of the study according to National Laws (Italian law nr.11960, released on 13/07/2004). Written consent was obtained from patients subjected to the surgical procedure and the treatment of data for scientific purposes.

Patients were recruited for this study between January 1997 and December 2017 and data were collected prospectively in a dedicated database employed for this study. All centers involved in this study applied the same study protocol and patient selection process. Study practices were homogeneous and outcome assessments centralized. During the same period of time the total number of patients undergoing various techniques of TAMR was 15,124. Patients receiving RITA on LAD, RITA on a right coronary branch, those with free or Y grafts, or those receiving a venous graft were excluded.

At the follow-up, both instrumental and clinical data were prospectively recorded in the database: hospital, physician or outpatient records, telephone interviews with the patients themselves or family members were collected.

Definitions and Study End Points

Primary endpoints of this study were: 1) Late death. 2) Repeat coronary revascularization (percutaneous coronary intervention [PCI] or repeat CABG). 3)

MACE, including cardiac death, nonfatal myocardial infarction (MI) or angina, target vessel revascularization, stroke and heart failure.

Postoperative myocardial infarction was diagnosed by troponin and ECG criteria [8]. The diagnostic and classification of diabetes mellitus (DM) were based on criteria suggested by the American Diabetes Association [10] and all patients with DM underwent strict glycemic control with preoperative continuous insulin infusion, insulin infusions during CPB and postoperative (24-48 hours) maintenance of blood glucose at <10 mmol/L. Obesity was classified [11] as class I for a Body Mass Index (BMI) between 30 and 34.9 kg/m2, class II for a BMI between 35 and 39.9 kg/m2, and class III for a BMI ≥ 40 kg/m2. Stroke was defined as a new onset of focal or global neurological deficit lasting more than 24 h. Definitions of chronic renal disease (CKD) and Chronic Obstructive Pulmonary Disease (COPD) were consistent with those of the Society of the Thoracic Surgeon Database.

Surgical Technique

Surgery was carried out as previously reported [12, 13]. Indication and contraindication for BITA was also the same as we have recently reported [13]: in summary patients with a reasonable life expectancy (>1year), those requiring minimization of aortic manipulation and the presence of at least two angiographically branches of the left coronary circulation which were graftable were included. Contraindications were: poorly controlled diabetes (defined as an uninterrupted HbA1c >8.0% for ≥1 year despite standard care [14], class III obesity, evolving or acute (6 hours to 7 days) myocardial infarction.

The target for skeletonized in situ LITA was the LAD and its branches. All patients had RITA on a left-sided target: in patients where two graftable branches were available, the branch with the larger perfusion area was selected; if both branches had identical perfusion areas, the distal branch was selected for RITA grafting, whilst the other vessel was re-vascularized with composite, sequential ITA grafts or other available conduits if required. In patients with heavily calcified aorta OPCAB-BITA represented first choice to reduce the operative risk.

Care was taken throughout the surgery to keep the pleurae closed, to preserve the pericardiacophrenic artery branches and to spare the communicating bifurcation of the ITAs to the wall of the chest. In cases where a radial graft was planned, the artery was harvested from the non-dominant arm after a preoperative assessment of the palmar arch with the Allen test. Digital plethysmography was carried out if required.
All interventions were carried out by four senior surgeons (M.B. E.P. G.S. and S.G.).

Postoperatively, careful control of the glycemic values was undertaken by employing continuous insulin infusion, giving certain consideration to the higher risk of deep sternal wound infection in BIMA employment [13]

Statistical Analysis.

To address missing values (range 0.002- 0.005) we used fully conditional specification multiple imputation method (1,000 replications).
Normality of data was assessed using the Kolmogorov-Smirnov test. Continuous data were summarized as mean (standard deviation) or median (twenty-fifth to seventy-fifth percentiles) in case of skewed distributions. Categorical variables were reported as counts and percentages and comparisons were carried out using Fisher's exact test.
Forty-two parameters (**Supplemental Material, Online Material**) were considered in the initial model. To enhance the accuracy of the model, the number of variables was reduced using variable clustering. All variables showing $p < 0.2$ at univariable analysis were introduced into multivariable analyses.

The Kaplan-Meier method and log-rank test were used for survival analysis. A Cox regression model was used to estimate predictors of death. The proportional hazard assumption was confirmed by use of Schoenfeld residuals. A competing risk analysis was used to avoid overestimation of the incidence of repeated revascularization and MACE. R, release 3.2.3 (R Foundation for Statistical Computing, Wien, Austria) software and "survival", "cmprsk" and "forestplot" packages were utilized. Significance for hypothesis testing was set at the 0.05 two-tailed level.

Results

In total**,** 1,325 patients underwent CABG by ISS-BITA-LLC-TAMR technique during the period of study and were included. During the same period of time the total number of patients undergoing various techniques of TAMR was 15,124. Preoperative characteristics are summarized in **Table 1.**

962 patients underwent on-pump arrested heart CABG and 363 patients underwent off-pump CABG. In the group undergoing on-pump CABG various types of myocardial protection strategies were employed in 355 patients: in the early stages of the study St Thomas' crystalloid cardioplegia was employed whilst after 2009 Custodiol was utilized. Also, cold blood cardioplegia was utilized in 607 patients.

Early Results

Early mortality was 1.4% (n=19) and the causes are shown in **Supplemental Material 2, Online Material** along with other early outcomes. Surgical data is given in **Table 2**. RITA was routed via the transverse sinus in 873 patients (66%) and behind the superior caval vein in 452 (34%). The number of distal anastomosis in patients undergoing off-pump was 2.5±0.8 versus 2.6±0.9 in on-pump group (P=0.06).

Thirty-three patients (2.5%) showed sternal wound infection and 12 (0.9%) of them required surgical treatment. Fifteen of these patients were diabetic, whilst 18 were not ($p>0.05$). Diabetes significantly increased mortality in patients with wound infection (9/15 60% vs. 0/18, $p<0.0001$).

Main Outcomes

There were 131 deaths during follow up (9.8%). Cumulative actuarial survival at 1, 5, 10, 15 and 18 years was 99.4± 0.2%, 97.5±2.3%, 93.1±5.7%, 85.7±7.8% and 62.6±9.3%, respectively (**Figure 1A**). When survival rates were further analyzed (**Figure 1B-E**) patients with LVEF≤ 35%, PVD, COPD (all, $p<0.0001$), ≥80 years ($p=0.0002$), and chronic kidney disease, (CKD, $p=0.0001$) all showed lower survival rates.

One-hundred-forty-six patients (11.0%) underwent repeat revascularization for graft failure: 16 (10.9 %) had redo CABG whereas 130(89%) underwent PCI. Also, in 57 of these patients revascularization occurred on another non-previously revascularized vessel. Eighty-five patients experienced RA failure (20.7% of RA), 39 a RITA failure (2.9% of RITA) and 22 (1.6% of LITA). Cumulative incidence of repeat revascularization at 1, 5, 10, 15 and 18 years (**Figure 2A**) was 2.3± 0.4%, 4.2±0.6%, 8.4±1.1%, 18.3±3.8% and 20.4± 5.5% respectively. Values were significantly higher in OPCAB and PVD patients (**Figure 2B, C**).

Median follow-up (100% complete) was 103 months (IQR 61 to 189 months) and ranged from 1 to 245 months. Cumulative follow-up was 156,424 patient-years.

Two-hundred-twenty-nine patients had MACE during the follow up (17.2%). Cumulative incidence of MACE was 2.6±0.4%, 5.1±0.7%, 11.3±2.1%, 26.3±6.4%, 32.4±8.0 % at 1, 5, 10, 15 and 18 years, respectively (**Figure 3A**). Cumulative incidence (**Figure 3B-F**) was higher in patients ≥ 80 years, with PVD, LVEF<35%, those undergoing off-pump surgery or with COPD. LVEF ≤ 35%, COPD, PVD (all, $p<0.0001$), CKD and age ≥80 years ($p=0.002$) were independent predictors of diminished long-term survival (**Table 3**). Competing risk analysis of PVD and OPCAB (both, $p<0.001$) predicted repeat revascularization whilst a number of factors were independent predictors of MACE (age ≥ 80 years, PVD, LVEF ≤ 35%, presence of OPCAB and COPD (all, $p<0.001$))

Discussion

The routine use of BITA has been hampered by a number of factors despite the reported benefits of a second ITA [3–6]. The majority of published studies are biased by significant differences including techniques, anastomose target and graft type.

In this paper we present a prospective 20-year experience in a relatively homogeneous population using a standard TAMR technique including in-situ skeletonized BITA for revascularization of left coronary branches and, when necessary, radial artery grafting for right coronary revascularization (ISS-BITA-LCC-TAMR).

In our population, incidence of long-term postoperative adverse outcomes was relatively low [6, 15], especially when considering duration of follow-up. We believe these results are likely linked to three technical factors: a) TAMR graft configuration; b) in-situ BITA arrangement (no Y free grafts) with a relatively small number of sequential anastomoses to ensure, in most of patients, the whole arterial flow to the main targeted vessel; c) both thoracic arteries anastomosed to the left circulation with LAD targeted by LITA and RITA never crossing the posterior sternum. Total arterial revascularization using BITA has previously been shown to be advantageous in terms of long-term survival, incidence of cardiovascular events, as well as reoperation and need for angioplasty [2, 16]. The influence of TAMR on outcomes is presumably linked to the higher over- time patency rate of arterial grafts and avoidance of vein graft atherosclerosis as well as the less extensive manipulation of the ascending aorta. It remains to be established whether, and how much, the positive influence of TAMR in our study dependent on the skeletonized technique graft design. Calafiore's group [17] previously reported that the long-term patency rate of skeletonized and pedicled ITA grafts was similar whereas other studies [18, 19] have shown that skeletonization of the ITA can improve conduit flow with larger vessel diameter. The recent ART trial [6, 20] has demonstrated the absence of any mid-term (5-year) benefit from BITA and that skeletonized harvesting did not add any further benefit compared to pedicled ITAs. However, only 48% of their patients received a skeletonized ITA with different configurations and, perhaps more importantly, follow-up was short. This could, at least in part, account for the differences seen with our study, as a recent study demonstrated that the differences between BITA and SITA only starts to become evident after 5 years [15]. At this time point results will also be influenced by the progressive reduction in the patency of vein grafts not employed in our study.

In-situ RITA has previously been shown to have similar patency rates as in-situ LITA [21, 22] hence, this configuration has the potential advantage that coronary bypass flow is dependent on both ITAs simultaneously, resulting in a lower risk of left ventricular hypo-perfusion. Other BITA configurations have significant drawbacks. The in-situ RITA to the LAD plus in-situ LITA to another left ventricular coronary artery leads to a high risk of damage during re-sternotomy [23]. The RITA as a free-graft has been demonstrated to have a low patency rate when this graft is connected proximally to the aorta [24]. In contrast, attachment of the free RITA to the in-situ LITA (T or Y graft) has previously been observed to improve patency [17]. This arrangement does not, however, apply to the principle that LV revascularization occurs from two different sources, which could represent a key issue for optimal revascularization. The in-situ LITA to LAD, and in-situ RITA to the other left coronary target vessel, avoids the difficulties of anastomosing a thin wall vessel (e.g. the free RITA) to a thick wall vessel (e.g. the aorta). Furthermore, it decreases the risks of injury in case of mediastinal revision or re-operation since both ITAs lie in a safe position, requiring a lower number of anastomoses being performed and, finally, offering the possibility to easily apply the "non-touch" principle, by using different graft configurations [3].

Accumulating evidence suggests that the LAD and circumflex territory revascularization should take priority over the RCA (in the majority of cases), as this vessel is not the clinical equivalent of the left-sided coronary branches [25, 26]. Nevertheless, a recent report failed (5) to identify differences in survival, repeat revascularization or combined outcomes between patients receiving RITA on left or coronary circulation in accordance with previous patient cohorts [26, 27] that had shown no differences in long-term outcomes when the RITA was anastomosed to the right or left coronary circulation. In contrast with these findings, other reports have suggested RITA grafting to the right coronary artery system may be less beneficial than to the left coronaries [20, 28]. Additionally, OPCAB was associated with increased risk of repeated coronary revascularization and MACE. According to our experience, OPCAB has to be taken into consideration in terms of risk of events during the follow-up period. This confirms previous data showing reduced graft patency, increased risk of cardiac re-intervention and death in CABG patients [29]. We can presume that among low-risk patients, adverse events related to cardiopulmonary bypass are rare and "technical adverse events", such as incomplete revascularization, diminished graft patency or reduced accuracy of anastomosis related to the technical challenge of OPCAB, may be responsible for the negative outcome. On the other hand, amongst higher-risk patients, CPB- and aortic manipulation- related events are more common and may outweigh technical adverse events. This may not be increased in higher-risk patients, since most patient comorbidities do not mean that OPCAB is more difficult to perform. Our findings must, however, be interpreted with caution, taking into consideration that the poorer outcome in OPCAB might be a result of higher disease burden. Furthermore, OPCAB techniques and facilitating devices have evolved over time hence our results may also be affected by our learning curve. Even taking this into account, the present findings suggest a "balanced" patient-centric approach should be utilised as has been advocated even by the ESC/EACTS in their 2018 Guidelines [9] with the balance shifted more towards OPCAB in patients with high risk of stroke, renal dysfunction, blood transfusion, respiratory failure and AF development as also suggested by the ISMIS Consensus Conference [29].

Finally, the link of diabetes to DSWI has been extensively studied and the prevalence of diabetes has been found to be three times higher among patients with DSWI than those without [2, 4, 6, 20] despite the fact that this patient population may have the most to gain from BITA grafting. Our data show that, with the skeletonized harvesting technique, diabetic patients did not have a significantly higher associated risk of DSWI although the mortality was significantly increased when patients presented with diabetes (60%, $p<0.0001$). This is in accordance with other studies [3, 4] and could be explained by the aggressive treatment received by our patients with well-established DM who are referred for CABG surgery (intravenous insulin infusion). An alternative hypothesis, however, could be that this is related to the accurate ITAs skeletonized harvesting technique where collateral blood flow to the sternum is preserved.

In Figure 4 we represent visually the advantage of the present surgical strategy in term of patients' survival: in this graph we compare long term survival with that of the ART trial[6] and of two other recent large studies [5, 30] with long-term follow-up employing only one thoracic artery and saphenous vein for myocardial revascularization

Limitations

A number of limitations need to be acknowledged, however. Firstly, the homogeneous population (representing one of the main strength of the paper) is also a drawback since it may introduce a selection bias (i.e. exclusion of with RITA on RCA because of ungraftable highly diseased circumflex artery, patients with a second ITA with additional saphenous vein grafts. etc.). Hence, we cannot exclude that this may contribute to the positive outcomes in this study, although the main risk factors of our BITA patients are comparable to those reported in previous studies [20].

Secondly, the study was underpowered by the low event rate. To overcome this limitation and increase power of the study we employed a variable-reduction method in our analysis. Fourthly, a direct comparison between single and double ITA as well as skeletonized vs. non-skeletonized technique was not carried out nor did we examine the true influence of skeletonized technique on long-term outcomes. Although these are all important points, they were points were beyond the main aim(s) of the present study. Thirdly, the target vessels were determined mainly by the perfusion area of the recipient artery and not selected randomly which may have introduced a bias. Finally, postoperative angiography was not routinely obtained meaning graft patency was unknown.

Conclusions

Coronary artery bypass using ISS-LITA-LCC-TAMR configuration resulted in satisfactory long-term results with low incidence of death and late events. Although our data does not provide a final answer regarding the potential benefits of using this approach in all patients, our findings encourage the use of this technique in selected CABG patients.

Conflict of Interest: The authors declare no conflicts of interest.

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Table 1. Patient Characteristics (n=1,325).

Females		284 (21.4%)
Mean age (years)		65.7±12.3
Range		28-87
Diabetes		329 (24.8%)
Hypertension		946 (65,3%)
Smoking		414 (71,4%)
Dyslipidemia		564 (42.6%)
CKD		
	Creatinine 120-250	69 (5.2)
	Creatinine >250	38 (2.8)
	Dialysis	16 (1.2)
Previous CVD		42 (3.2%)
PVD		111 (8.4%)
COPD		
	Mild- FEV_1<50% predicted	79 (5.9 %)
	Moderate- FEV_1<50-59 predicted	43 (3.2%)
	Moderate- FEV_1<50-59 predicted	5 (0.3%)
NYHA		1.7±0.9
CCS		3.2±0.8
Stable angina		759 (57.3%)
Unstable angina		566 (42.7%)
Prior myocardial infarction		712 (53.7%)
Prior coronary angioplasty		428 (32.3%)
Preoperative IABP		168 (12.6)
Heavily calcified aorta		123 (9.3%)
Coronary angiography data		
	Three- vessel disease	925 (69.8%)
	Two-vessels disease	329 (24.8%)
	Left main coronary artery stenosis	441 (33.3%)
LVEF		51.6±9.3
LVEF ≤ 35%		301 (22.7%)
EUROSCORE II		2.9±0.8
STS Score		3.6±2.7

Data are shown as mean ± SD or numbers (percentage). Abbreviations: CKD: Chronic Renal Disease; CVD: Cerebrovascular Disease; PVD: Peripheral Vascular Disease; COPD: Chronic Obstructive Pulmonary Disease; FEV_1: Forced Expiratory Volume in 1 second; NYHA: New Heart Association functional class; CCS: Canadian Cardiovascular Society angina class; IABP: Intra-aortic Balloon Pump; LVEF: Left Ventricular Ejection Fraction; STS: Society of Thoracic Surgeons. Heavily calcified aorta: Aorta with the ascending portion circumferentially calcified, detected at Thoracic Rx Thoracic TC Scan or detected manually during the surgical inspection at the operation time.

Table 2. Operative Data (n=1,325).

Urgent/Emergent	379 (28.6%)
REDO	77 (5.8%)
Cardiopulmonary bypass time (minutes)	83.7±21.3
Aortic cross-clamping time (minutes)	64.6±16.4
Off-pump coronary artery bypass grafting	363 (27.4%)
Number of distal anastomoses per patients	2.6±0.7
Coronary artery endarterectomy	104 (7.8%)
Sequential anastomoses in-situ LITA-LAD-DA	365 (27.5%)
Sequential anastomoses in-situ LITA-DA-LAD	257 (19.4%)
RITA Grafted to the IA	238 (18%)
RITA Grafted to the OM	822 (62%)
RITA Grafted to the PL	265 (20%)
Sequential anastomoses in-situ RITA	19 (1.4%)
Radial artery on RCA or one of its branches	410 (30.9%)

Data are shown as mean ± SD or numbers (percentage). Abbreviations: LITA= Left Internal Thoracic Artery; DA= diagonal branch of left descending artery; LAD: Left Descending Artery; RITA= Right Internal Thoracic Artery; IA= Intermediate artery; OM= obtuse marginal artery; PL= Postero-Lateral branch of the circumflex artery; RCA= Right Coronary Artery; DSWI= deep sternal wound infection.

Table 3. Predictors of Main Outcomes.

	HR	95% CI	p
Death			
LVEF<35%	11.71	5.65 to 24.27	<0.001
COPD	4.27	2.37 to 7.67	<0.001
PVD	14.84	6.70 to 32.89	<0.001
CKD	3.40	1.82 to 6.37	<0.001
Age≥80 years	2.79	1.64 to 4.75	<0.001
DM	2.53	0.79 to 17.52	0.089
ID-DM	3.28	0.90 to 31.86	0.069
3-vessel Disease	2.76	0.61 to 18.83	0.093
	SHR	**95% CI**	**p**
Repeat Revascularization			
OPCAB	17.42	6.35 to 47.32	<0.001
PVD	8.78	4.23 to 19.34	<0.001
MACE			
Age≥80 years	2.45	1.75 to 3.94	<0.001
PVD	8.55	4.23 to 14.88	<0.001
LVEF < 35%	14.21	6.47 to 30.54	<0.001
OPCAB	2.12	1.07 to 3.54	<0.001
COPD	1.89	1.13 to 3.41	<0.001
Female sex	2.05	0.67 to 7.77	0.069
CVD	3.04	0.75 to 25.05	0.064
CKD	4.55	0.67 to 10.85	0.078

Abbreviations: HR: Hazard Ratio; DM: Diabetes Mellitus; COPD: Chronic Obstructive Pulmonary Disease; LVEF: Left Ventricular Ejection Fraction; CKD: Chronic Renal Disease; PVD: Peripheral Vascular Disease; ID-DM: Insulin Dependent Diabetes Mellitus; MACE: Major Adverse Cardiovascular Events; OPCAB: Off-Pump Coronary Artery Bypass. CVD: Cerebral Vascular Disease

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Figure Legends

Central Picture. Picture summarizing the surgical strategy applied.

Figure 1. Overall Survival and Survival in sub-groups of patients. Abbreviations: LVEF: Left Ventricular Ejection Fraction; PVD: Peripheral Vascular Disease; COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease. Of note is the Kaplan Meir curves are plotted from 70-100% survival probability in Panel A and from 10-100% survival probability in Panel E. All other curves are plotted from 0-100% survival probability.

Figure 2. Total cumulative incidence of repeat revascularization and stratified by groups. Abbreviations: OPCAB: Off-pump Coronary (Artery) Bypass; PVD: Peripheral Vascular Disease.

Figure 3. Total cumulative incidence of MACE and by sub-groups. Abbreviations: PVD: Peripheral Vascular Disease; LVEF: Left Ventricular Ejection Fraction; OPCAB: Off-pump Coronary (Artery) Bypass; COPD: Chronic Obstructive Pulmonary Disease;

Figure 4. Graphic comparison demonstrating the benefit obtained whit Bilateral-ITA vs Monolateral-ITA: our long-term survival curve is related with the ART trial[6] and another two Monolateral-IMA long-term studies survival curves [5, 30]. Of note is the Kaplan Meir curves are plotted from 75-100% survival probability

Abbreviation List

I SS-LITA-LCC-TAMR: in-situ skeletonized bilateral thoracic artery for left coronary circulation

LITA: Left Internal Thoracic Artery

RITA Right Internal Thoracic Artery

BITA: Bilateral Internal Thoracic Artery

RA: Radial Artery

SVG: Saphenous venous graft

CKD: Chronic Renal Disease;

CVD: Cerebrovascular Disease;

PVD: Peripheral Vascular Disease;

COPD: Chronic Obstructive Pulmonary Disease;

FEV_1: Forced Expiratory Volume in 1 second;

NYHA: New Heart Association functional class;

CCS: Canadian Cardiovascular Society angina class;

IABP: Intra-aortic Balloon Pump;

LVEF: Left Ventricular Ejection Fraction;

STS: Society of Thoracic Surgeons.

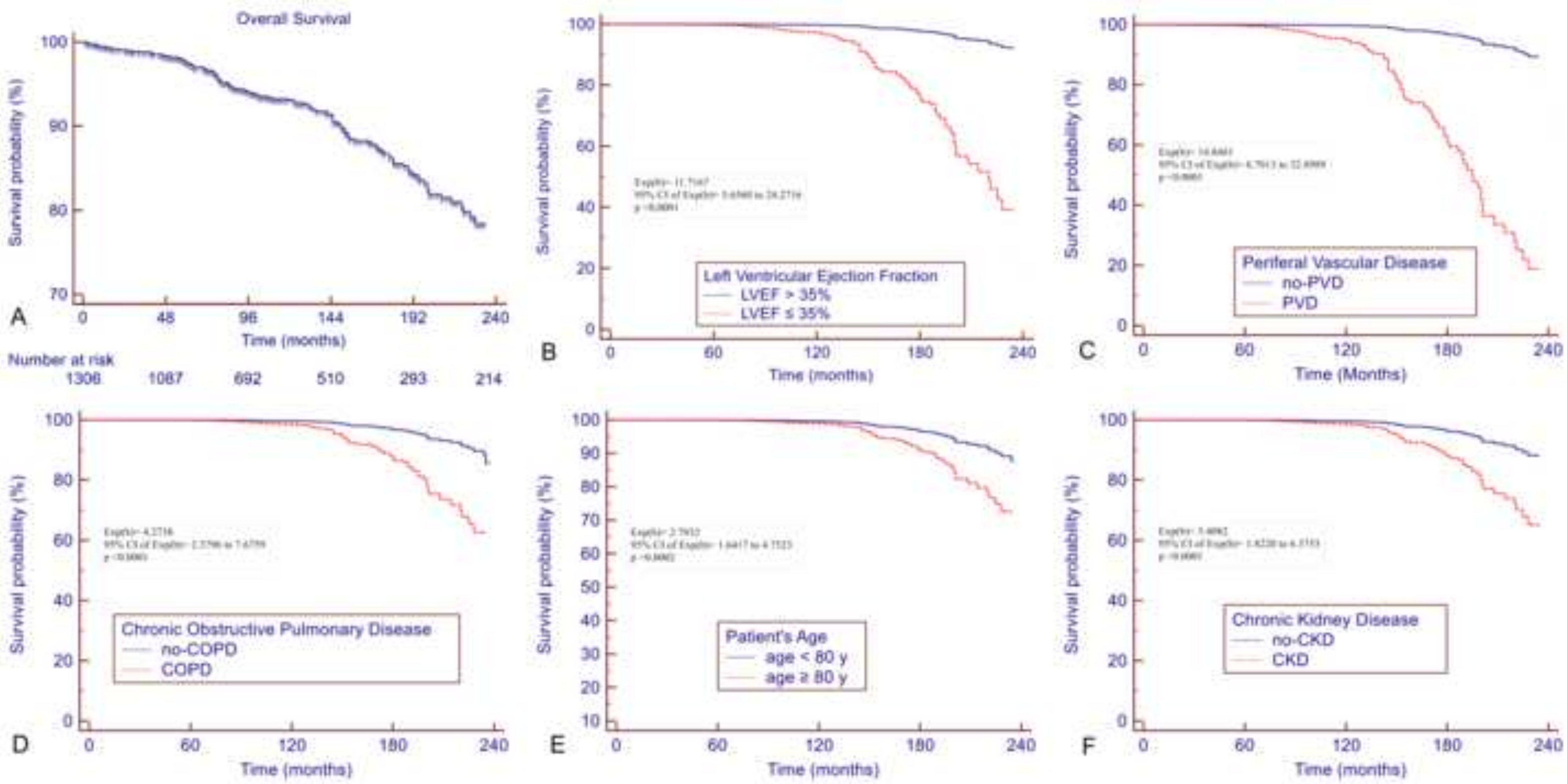
DM: Diabetes Mellitus;

ID-DM: Insulin Dependent Diabetes Mellitus;

MACE: Major Adverse Cardiovascular Events;

OPCAB: Off-Pump Coronary Artery Bypass.

Figure 1



Overall Survival
Survival probability (%)
100
90
80
70
A
0
48
96
144
192
240
Time (months)
Number at risk
1306
1087
692
510
293
214
B
Survival probability (%)
Left Ventricular Ejection Fraction
LVEF > 35%
LVEF ≤ 35%
Time (months)
C
Survival probability (%)
Periferal Vascular Disease
no-PVD
PVD
Time (Months)
D
Survival probability (%)
Chronic Obstructive Pulmonary Disease
no-COPD
COPD
Time (months)
E
Survival probability (%)
Patient's Age
age < 80 y
age ≥ 80 y
Time (months)
F
Survival probability (%)
Chronic Kidney Disease
no-CKD
CKD
Time (months)

Figure 2

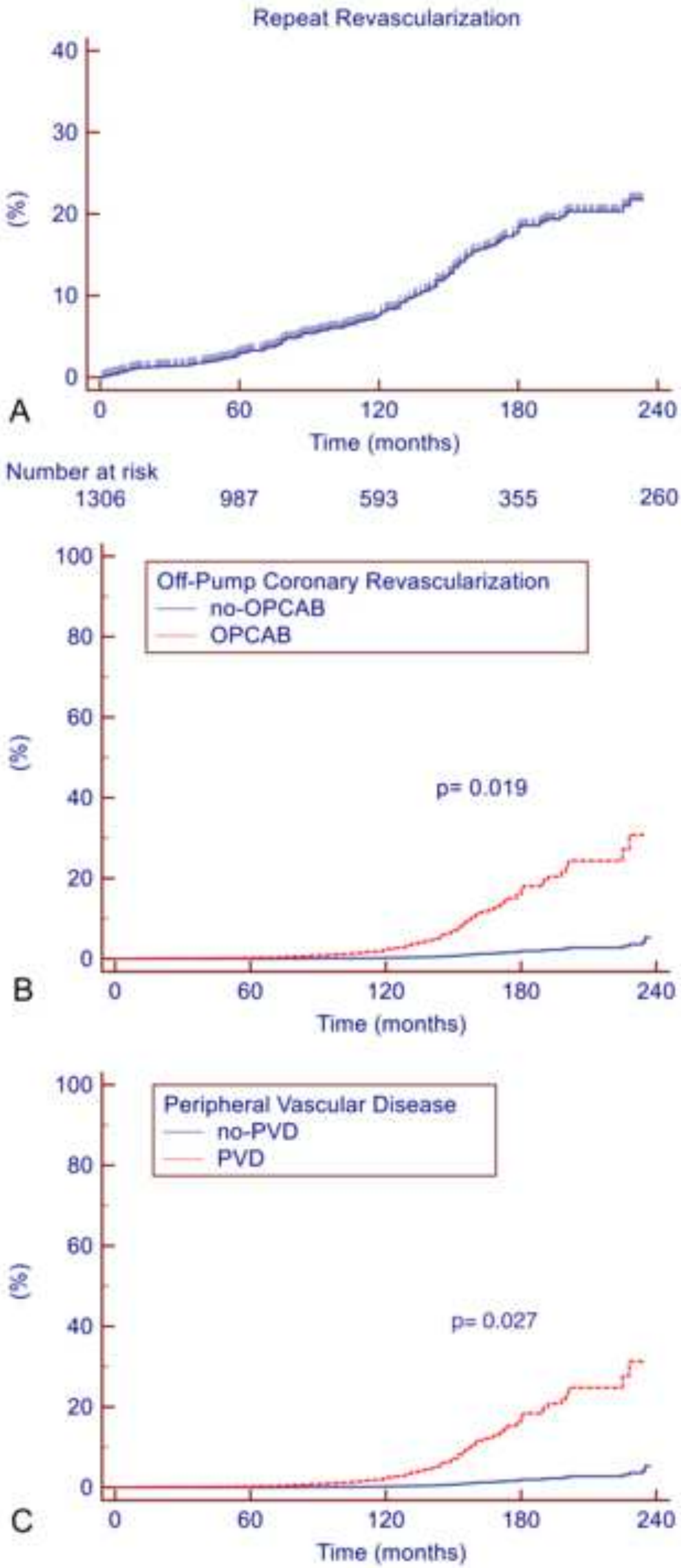

Repeat Revascularization
(%)
40
30
20
10
0
A
0
60
120
180
240
Time (months)
Number at risk
1306
987
593
355
260
100
80
60
40
20
0
Off-Pump Coronary Revascularization
no-OPCAB
OPCAB
(%)
p= 0.019
B
0
60
120
180
240
Time (months)
100
80
60
40
20
0
Peripheral Vascular Disease
no-PVD
PVD
(%)
p= 0.027
C
0
60
120
180
240
Time (months)

Figure 3

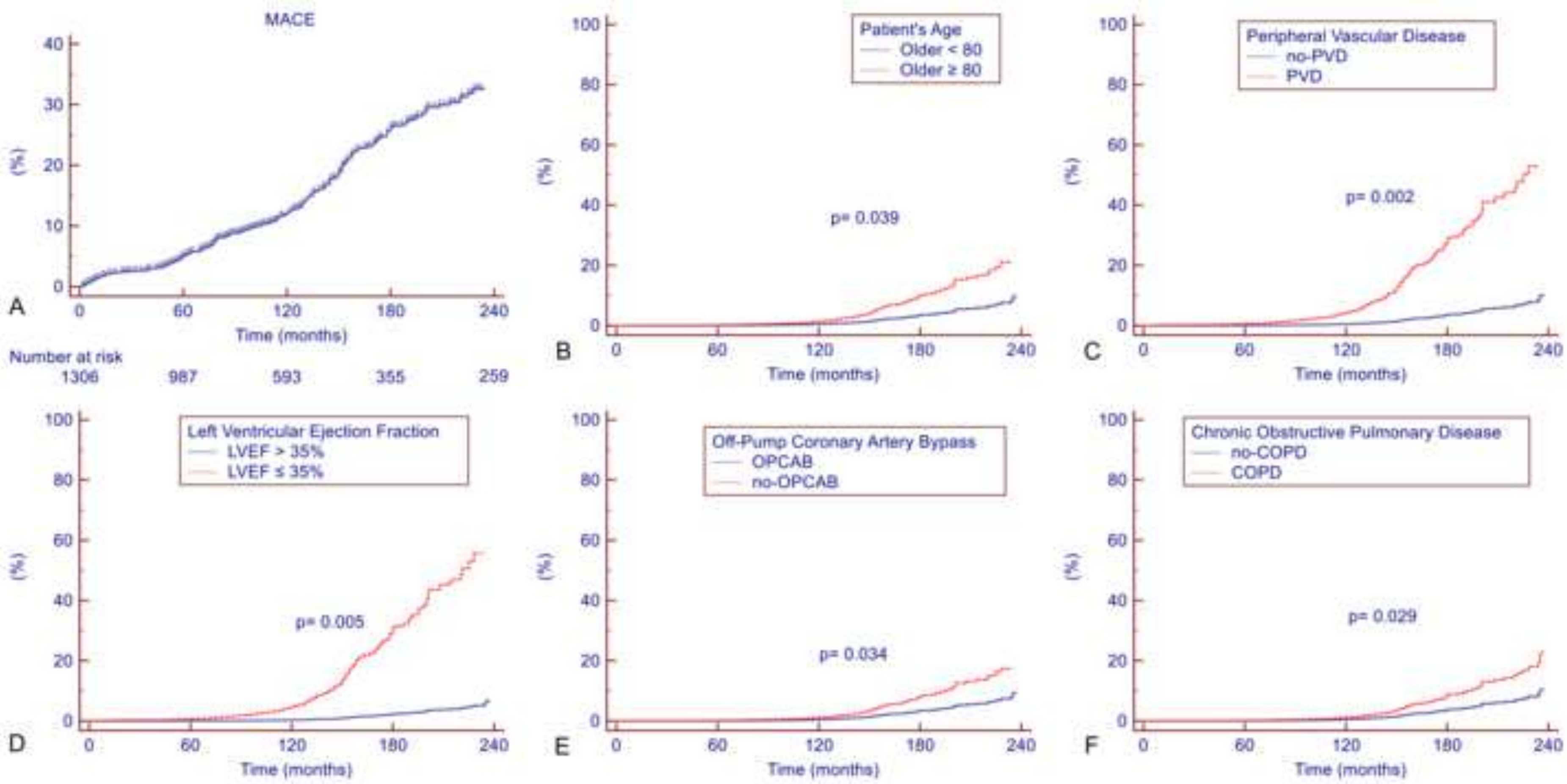
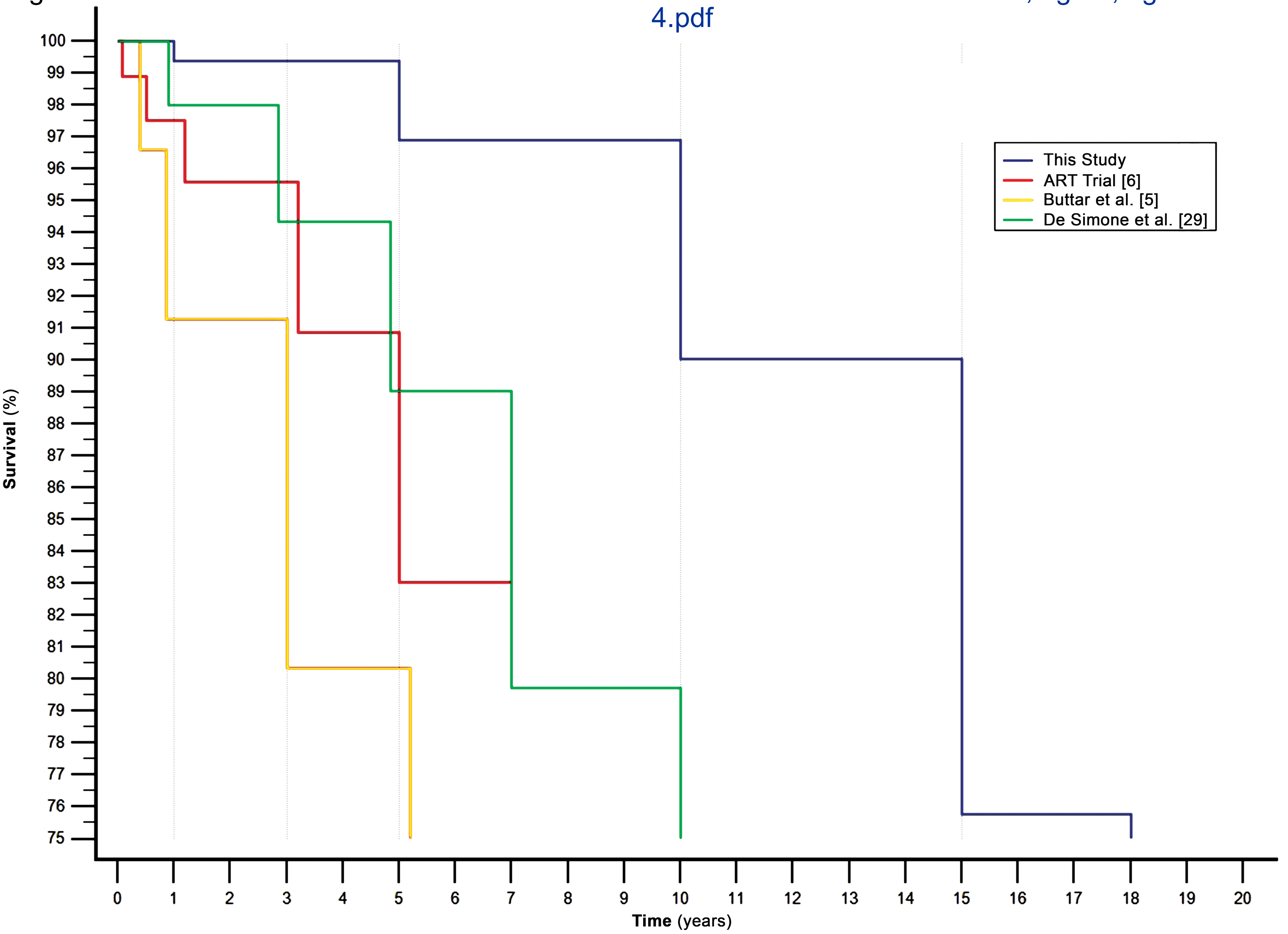

MACE
(%)
A
Time (months)
Number at risk
1306
987
593
355
259
B
Patient's Age
Older < 80
Older ≥ 80
p= 0.039
C
Peripheral Vascular Disease
no-PVD
PVD
p= 0.002
D
Left Ventricular Ejection Fraction
LVEF > 35%
LVEF ≤ 35%
p= 0.005
E
Off-Pump Coronary Artery Bypass
OPCAB
no-OPCAB
p= 0.034
F
Chronic Obstructive Pulmonary Disease
no-COPD
COPD
p= 0.029

Figure 4



This Study
ART Trial [6]
Buttar et al. [5]
De Simone et al. [29]
Survival (%)
100
99
98
97
96
95
94
93
92
91
90
89
88
87
86
85
84
83
82
81
80
79
78
77
76
75
Time (years)
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20